

**N2pc Modulation as an Electrophysiological Marker of Output-Based
Inhibitory Cueing Effects**

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Statement of Sources

I declare that this report is my own original work and that contributions of others
have been duly acknowledged.

Sean Skerratt

Date:

Dedication

I would like to dedicate the completion of this work to the memory of Liam Burnie.

His is a friendship I will not soon forget.

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First and foremost, I would like to thank my supervisor, Dr. Jason Satel. I am sincerely grateful for the continuing guidance and support he has offered throughout the past year. Thanks must also go to Alfred “code-master” Lim, Joel, Jess, and Chelsea whose contributions to this project were invaluable.

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Table of Contents

Statement of Sources.....	ii
Dedication	iii
Acknowledgements	iv
Table of Contents	v
List of Figures	vii
Abstract	1
IOR in Spatial Cueing Tasks.....	3
Inhibitory Cueing Effects.....	4
Input-Based ICEs	5
Output-Based ICE	7
Reconceptualising IOR	9
Electrophysiological Markers of ICEs	10
The P100 Cueing Effect	10
Posterior-Contralateral N2 (N2pc).....	12
Attentional Deficits	14
Study Rationale & Aims	15
Hypotheses	16
Method	17
<i>Participants</i>	17
<i>Design</i>	18
<i>Materials</i>	18
Eye tracking.....	18
Electroencephalography	18
Spatial Cueing Task.....	18
<i>Procedure</i>	20
<i>Analysis</i>	22
Results	23
<i>Behavioural Results</i>	23
<i>N2pc Results</i>	24
Discussion	26
<i>Behavioural</i>	26
<i>Electrophysiological</i>	30
<i>Limitations</i>	35

<i>Future Directions</i>	36
<i>Summary and Conclusions</i>	37
References	40
<i>Appendix A</i>	49
<i>Appendix B</i>	51
<i>Appendix C</i>	53
<i>Appendix D</i>	54

List of Figures

<i>Figure 1. Example of a typical spatial cueing task.....</i>	<i>4</i>
<i>Figure 2. Grand mean waveforms showing an N2pc.....</i>	<i>13</i>
<i>Figure 3. Time course of the spatial cueing task used in the present study.....</i>	<i>20</i>
<i>Figure 4. Mean reaction times for cued and uncued trials across oculomotor-state</i>	<i>24</i>
<i>Figure 6. Grand mean waveforms (uncued-cued) for control in active state.....</i>	<i>25</i>
<i>Figure 5. Grand mean waveforms (uncued-cued) for control in suppressed state....</i>	<i>25</i>
<i>Figure 7. Grand mean waveforms (uncued-cued) for deficit in active state</i>	<i>26</i>
<i>Figure 8. Grand mean waveforms (uncued-cued) for deficit in suppressed state</i>	<i>26</i>

Abstract

An inhibitory cueing effect (ICE) is a phenomenon whereby behavioural responses (such as a manual keypress or saccade) to stimuli appearing at recently attended locations are slowed, provided that time elapsed is sufficient for the extinction of early facilitation effects. This phenomenon, often referred to as inhibition of return (IOR), is thought to be a functional component of visual search which facilitates novelty seeking. Research has demonstrated two dissociable mechanisms underlying ICEs – input-based and output-based. The present study used a modified spatial cueing task with both active and suppressed oculomotor-states, combined with electroencephalography (EEG) measurement, to investigate whether the deployment of covert visual attention (measured as the amplitude of N2pc) is modulated differentially by input and output-based ICEs. Additionally, the present study sought to examine the effect of attentional deficits on both behavioural inhibition (manual response times) and the modulation of deployed attention. Behavioural results showed that ICEs were elicited, however the observed inhibition was identical across oculomotor-state. The effect of group was marginally significant, with post-hoc analyses revealing a significant difference between uncued and cued targets in the control group (slower to cued), but only marginal significance for the deficit group. No significant results were found for N2pc analyses, however a polarity inverse to that expected was observed. Results, interpretations, and recommendations for future research are discussed.

Inhibition of return (IOR) is a phenomenon whereby behavioural responses to stimuli appearing at recently attended locations are inhibited, provided that time elapsed is sufficient for the extinction of early facilitation effects (Posner & Cohen, 1984; for a review, see Klein, 2000). It has been conceptualised as an inhibitory mechanism that facilitates novelty seeking in visual search by way of biasing an individual's attention toward novel salient stimuli (Posner, 1984; Posner, Rafal, Choate, & Vaughan, 1985). From an evolutionary perspective, this inhibition is proposed to have developed as a means by which the detection of task-relevant stimuli is prioritised through the biasing of attention away from areas that were previously attended (Klein, 2000). In a practical sense that harks back to the lifestyle of our ancestors, it has been described as being a mechanism of visual search which aids in the foraging of food and detection of threats (Klein, 1988).

This functional explanation of IOR was explored by Klein (1988) in the context of complex visual search tasks which required the participant to locate a target amongst multiple distractors. Because of the similarities between the distractors and the target itself, such tasks – referred to as serial searches – require the participant to inspect each item in a procedural manner, demanding the allocation of attention. Klein (1988) proposed that upon orienting of attention to a target requiring inspection, a subsequent inhibitory ‘tagging’ of that location would reduce the likelihood of re-attention, thus promoting inspection of areas not already attended (i.e., novel). To test this, Klein (1988) examined the response times (RTs) of participants to illuminated pixels (probes) presented following either easy (pre-attentive) or difficult (requiring serial search) visual search tasks. In line with his hypothesis, Klein (1988) found that the detection of probes appearing at locations previously inspected was delayed in comparison to those which appeared in a novel

location, but only subsequent to serial search. These findings, since replicated (Klein & MacInnes, 1999; Wang & Klein, 2010), show the presence of inhibition under conditions demanding the allocation of attention, supporting the notion of IOR as an attentional mechanism which facilitates visual search, and lending credence to its conceptualisation as a foraging facilitator.

IOR in Spatial Cueing Tasks

Within a research context, the IOR is most commonly investigated in tasks of spatial cueing which serve to orient the attention of participants (Martín-Arévalo et al., 2014; Satel, Hilchey, Wang, Reiss, & Klein, 2014). In such tasks, participants are presented (via a computer display) with a stimulus (pixel-width, or luminance change) that is non-predictive of the future location of a target. Whilst this stimulus is non-predictive, within the paradigm it is referred to as a cue. It is important that the cue does not provide information about where the target is going to appear. This is because when a cue informs a target's location, a participant will quickly pick up on the pattern and they will be more likely to adopt strategies which will result in an increased rate of correctly anticipating its appearance (i.e., attentional orienting becomes facilitated; Bonato, Lisi, Pegoraro, & Pourtois, 2018)

A trial within a typical spatial cueing task involves a central fixation square in the middle of a computer monitor, flanked by two placeholder squares (see Figure 1). All three squares remain in their positions for the duration of each trial. A non-predictive cue is then presented on either the left or right side of fixation at random (50/50, or chance frequency). Typically, this cue is an enlargement of the pixel width of the lines comprising the placeholder box.

Participants then either move their eyes to the cue location and back to the point of fixation or remain fixated and rely on peripheral vision (Taylor & Klein,

2000). This is followed by a target which appears left or right (50/50 again), to which participants are asked to respond as quickly and accurately as possible through either manually pressing a corresponding key, or through saccadic movement of the eyes to the target (i.e., behavioural responses). In such tasks, a target that has, through chance, been preceded by a cue on the same side is referred to as a cued target, whereas a target appearing on the side opposite is termed uncued (Klein, 2000).

Inhibitory Cueing Effects

In tasks of spatial cueing, when the time between the onset of the cue and the onset of the target – a time differential known as cue-target onset asynchrony (CTOA) - is less than approximately 300ms, behavioural responses are facilitated, and so reaction times decrease (Klein, 2000). However, when the CTOA is greater than approximately 300ms, a delayed behavioural response is observed for cued targets in comparison to uncued (Klein, 2000; see Figure 1). This delay in RT, as a whole, is referred to as an inhibitory cueing effect (ICE) – a relatively recent term proposed to describe both sensory and attentional inhibition occurring in visual search, and tasks of spatial cueing (Hilchey et al., 2014).

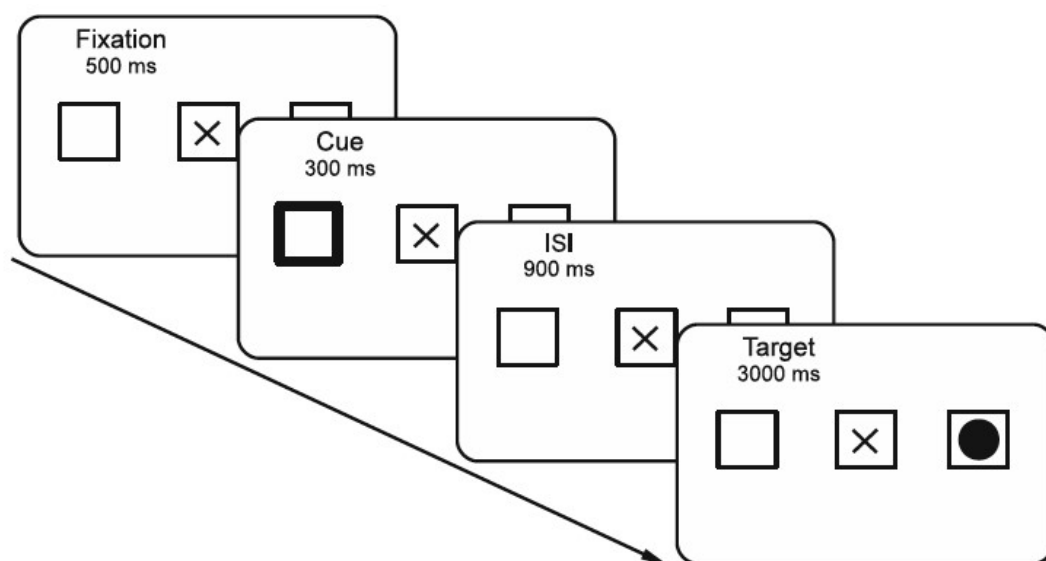


Figure 1. An uncued target trial in a typical spatial cueing task with a CTOA of 1100ms (cue + ISI). (Satel, Hilchey, Wang, Story, & Klein, 2013)

In the past, the term IOR has been used liberally to describe all ICEs on target responses observed following cue presentation in a spatial cueing context. However, a growing body of research suggests that there are, in fact, two discrete inhibitory mechanisms underlying overall behavioural inhibition (Hilchey et al., 2014). These two mechanisms have been categorised as input-based (modulating early sensory and perceptual processing), and output-based (modulating response processes; Hilchey et al., 2014; Taylor & Klein, 2000). In recent years, separate, yet converging, lines of inquiry have demonstrated that these two mechanisms are able to be dissociated, suggesting that there are two distinct systems by which an ICE can be elicited (Sumner, Nachev, Vora, Husain, & Kennard, 2004; Fecteau & Munoz, 2005).

Input-Based ICEs

Input-based ICEs are those proposed to modulate early sensory and perceptual processing. An influential, and often studied, source of input-based ICE generation is sensory adaptation (Dukewich, 2009; Satel, Wang, Trappenberg, & Klein, 2011).

Sensory adaptation refers to a decrease in stimulus detection resulting from repetitive stimulation (Dukewich, 2009). This process is seen to reflect neuronal fatigue resulting from recurrent stimulation and, as such, is considered to be an early-input stage process (Dukewich, 2009). Evidence for the role of sensory adaptation comes from studies examining neuronal activity in the superficial and intermediate layers of the superior colliculus (sSC, iSC, respectively; Fecteau & Munoz, 2005). The layers of the sSC are seen to represent visual neurons, whereas layers of the iSC represent visuomotor neurons (White et al., 2017). In a study examining the neural correlates of IOR in rhesus monkeys, Fecteau and Munoz (2005) found that reduced activity within the sSC, resulting from neuronal fatigue, played a role in generating

an inhibitory response to cued targets both when eye-movements were required, and when they were suppressed. When eye-movement was required, however, activity in the layers of the iSC was found correlate more strongly ($r = .38$) with behavioural inhibition than the visual neurons of the sSC ($r = .09$; Fecteau & Munoz, 2005). These findings are consistent with the proposal of a sensory refraction origin of inhibition when the oculomotor system is suppressed (input-based ICEs), and the co-occurrence of a sensory refraction *and* visuo-attentional inhibitory mechanism when the system is active (output-based ICEs; Fecteau & Munoz, 2005; Satel et al., 2013). Further dissociations between input and output-based inhibition have also been found through the use of short-wave (SW) light frequencies, a type of light that bypasses the SC (Sumner et al., 2004). Sumner et al. (2004) examined this SW frequency, along with normal luminance cues, in a spatial cueing task which used peripheral cues and had both an oculomotor active and suppressed state condition. They found that, in the suppressed state, when participants were required to respond to the target by way of a keypress, ICEs were observed across both light-wave types (Sumner et al., 2004). However, when a saccadic response to the target was required, an ICE was observed for normal luminance but not SW frequencies. Such findings indicate that inhibition of this nature can be observed without mediation by the SC, but *only* when the oculomotor system is not active (Sumner et al., 2004). This further supports the proposal that there are two distinct pathways leading to ICEs, with oculomotor activation as being necessary in the generation of one (i.e., output-based).

Evidence to support the notion that a sensory adaptation component has the capacity to contribute to ICE generation can also be seen in behavioural outcomes of modified spatial cueing tasks. Dukewich and Boehnke (2008) examined the effect of presenting of one, or multiple (up to five) cues, sequentially, prior to a target

response. Findings of this study showed that an increase in the number of cues preceding a target resulted in a corresponding delay in participant RTs for cued targets – an effect not observed for uncued targets (Dukewich & Boehnke, 2008). That is, under conditions where sensory adaptation is purposefully made to occur by repetitive stimulation, inhibition was observed, and its strength increased with the number of stimulations.

Output-Based ICE

In a series of experiments looking at the role of oculomotor activation in inhibition over differing CTOA time-courses, Hilchey et al. (2014) employed a spatial cueing task which presented participants with either a peripheral or central arrow target. For both target types, participants fixated on a central location, then, after 500ms, a peripheral non-predictive cue was presented which they were instructed to ignore. Following this, one of the two target types was presented. For peripheral targets, participants were to make a fast, accurate, eye movement to the target location. In the event of a central arrow target, participants were required to saccade to the side of the screen corresponding to the direction of the arrow. The behavioural RT (manual response/saccadic response) data was categorised into either cued or uncued, with difference scores calculated to determine the presence of inhibition (i.e., scores significantly differing from zero; Hilchey et al., 2014).

They found that, at a short CTOA (<450ms) saccadic responses to peripheral targets displayed ICEs, while those made to central arrow targets showed brief facilitatory cueing effects (Hilchey et al., 2014). Put another way, peripherally cued peripheral targets displayed an ICE, while peripherally cued central arrow targets did not, suggesting inhibition along the input pathway. In contrast, when the CTOA was longer (1050ms), saccadic responses to cued targets were indistinguishably slowed

(Hilchey et al., 2014). That is, at this CTOA it appears that the facilitatory effect observed reverses such that the cue elicits an effect on the output pathway (i.e., an output-based ICE) regardless of whether peripheral or central stimuli are used. Conversely, when oculomotor-state was suppressed, an ICE at the 1050ms CTOA was only observed for peripheral targets, reflecting, again, an input-based inhibition (Hilchey et al., 2014). Taken together, they posited that the statistical similarity observed (at the long CTOA) across target type when oculomotor activation was present suggests the presence of inhibition along input *and* output pathways. Equally, the presence of only peripheral target inhibition at the same CTOA when the oculomotor system was suppressed suggests that output-based ICEs are conditional on the activation of the oculomotor system (Hilchey et al., 2014).

These findings are consistent with the findings of a study by Rafal, Calabresi, Brennan, and Sciolto (1989), in which participants were asked to either remain fixated, make a saccade, or prepare a saccade to a peripheral or central arrow target. In designing the study, Rafal et al. (1989) drew upon the findings of Posner and Cohen (1980), who found that an un-informative peripheral cue primes the oculomotor system to prepare an eye movement. Rafal et al. (1989) hypothesised that long-CTOA inhibition, affecting peripherally cued targets, might share an underlying mechanism – the activation of the oculomotor system. What they found was that, not only were ICEs observed in conditions where participants made saccades to cues, but they were also observed in the condition that merely required them to *prepare* a saccade. These findings, taken together with those of Fecteau and Munoz (2005), provide converging evidence in support of a distinct, output-based mechanism of inhibition that is conditional on the oculomotor system being active.

Reconceptualising IOR

Converging lines of research suggest a dissociation between input and output-based mechanisms that generate ICEs. Given the way in which they manifest differently across CTOA and oculomotor-state, it seems prudent to reorient the discussion of inhibition within spatial cueing paradigms. At this point, the meaning of the term IOR seems to be relative to the subjective interpretation of the researcher discussing it. In a study which illustrates this point, a survey of 37 experts (four or more publications on the topic) querying the components they deemed necessary to term an effect IOR, found that not one criterion was endorsed unanimously (Dukewich & Klein, 2015). Moreover, Dukewich and Klein (2015) reported that 57% of respondents agreed that IOR is an umbrella term used to describe effects of a similar nature, with the remaining 43% of the opposite opinion. Because output-based ICEs have been proposed to occur only in the wake of oculomotor activation, this term will henceforth be used to describe an inhibitory effect on behavioural responses to cued targets which involve the making (or preparation) of a saccade. Equally, any ICE occurring in the absence of oculomotor activation will be referred to as an input-based ICE.

Taken together, the body of existing literature suggests that ICEs observed in un-informative spatial cueing tasks (often referred to as IOR) can be categorised as input or output-based depending upon the activation state of the oculomotor system (and CTOA). Evidence for a dissociation between the two suggests that divergent neural pathways modulate behavioural responses to cued targets by way of sensory adaptation and direct inhibition (e.g., Fecteau and Munoz, 2005; Sumner et al., 2004). Further, while sensory adaptation is observed when the oculomotor system is active and suppressed, evidence suggests that in an active state this neural refraction

combines with a mechanism of direct inhibition resulting in the greater inhibition observed when compared to suppressed state ICEs (Hilchey et al., 2014; Satel et al., 2013).

Electrophysiological Markers of ICEs

In the search for an electrophysiological marker of ICEs, recent research has begun integrating brain imaging techniques with spatial cueing tasks (e.g., Maheux & Jolicœur 2017; Mertes, Wascher, & Schneider, 2016). As this phenomenon occurs within a time-period that ranges from 300ms to several seconds, event-related potentials (ERPs) have become a useful tool in investigating the temporal dynamics of its action due to the high-temporal resolution they afford (Satel, Hilchey, Wang, Story, and Klein, 2013). However, a reliable electrophysiological marker has, thus far, proven to be elusive (Satel, Hilchey, Wang, Reiss, & Klein, 2014).

An ERP is an average of Electroencephalograph (EEG) traces, time locked to the onset of a stimulus (Woodman, 2010). These averages are used in examining the amplitude of post-synaptic neural activity in general areas of the brain at specific points in time (Bruyns-Haylett et al., 2017). An ERP component is a positive (P) or negative (N) peak occurring within specific time intervals after stimulus onset (Woodman, 2010). The names of such components are derived from a combination of their polarity and onset time and are often seen to reflect particular neural processes (Luck et al., 2000).

The P100 Cueing Effect

Of particular interest to researchers investigating the neural correlates of ICEs is an ERP known as P100 (or P1), and its modulation when examined as part of a spatial cueing task (referred to as the P1 cueing effect). The P1 is a component which reflects early sensory processes (Dias, Butler, Hoptman, & Javitt, 2011). The P1

cueing effect describes a common finding in tasks of spatial cueing, wherein peripheral cues modulate neuronal activity in early visual processing; this modulation results in a reduced P1 amplitude for cued targets as opposed to uncued (McDonald, Hickey, & Green, 2009).

Investigating the distinction between input and output-based mechanisms of inhibition, and its conditionality on oculomotor activation, Satel, Hilchey, Wang, Story, & Klein (2013) sought to examine the P1 cueing effect in a spatial cueing task involving both eye movement (active) and no eye movement (suppressed) conditions. In the active condition, participants were instructed to make a saccade to the cue, return to fixation, and respond with a localisation keypress. At a CTOA of 1200ms, Satel et al. (2013) found greater inhibition (i.e., slower responses) for cued targets over uncued, consistent with the literature. Additionally, they found a significant interaction between condition and cue such that responses were more than twice as slow in the active condition than the suppressed, indicating that the oculomotor activation resulted in additional inhibition (Satel et al., 2013). This finding has been cited as possible evidence for the occurrence of a separate inhibitory mechanism (i.e., output-based) when the oculomotor system is in an active state (Hilchey et al., 2014).

Interestingly, while a P1 cueing effect was observed in both conditions, it was significantly correlated (negatively) with behavioural inhibition (RTs) *only* when the oculomotor system was suppressed (Satel et al., 2013). What this suggests is that while the P1 cueing effect is present in both input and output-based ICEs, this is likely due to sensory adaptation, and as such this effect does not accurately reflect the proposed inhibitory attentional mechanism responsible for output-based ICEs (Satel et al., 2013). Due to this fact, it is not likely that P1 is a viable neural marker of output-based ICEs.

Posterior-Contralateral N2 (N2pc)

McDonald et al. (2009) endeavoured to control for non-attentional processes (e.g., sensory adaptation) in order to clarify the degree to which later attentional processes are modulated by ICEs. To achieve this, they employed a spatial cueing task with a target-target stimulus display consisting of two, separate, coloured discs. The target display was preceded by a target-indicator screen (a single coloured disc) which served to identify which of the three possible discs was the impending target. Such a design is similar in ways to a typical spatial cueing task, however, instead of the peripheral target appearing on its own, it was presented simultaneously with a ‘distractor’ of equivalent size and structure (in this case only dissimilar in colour) which the participant was to ignore. This is what is referred to as a discrimination task, in that the participant is required to differentiate between the two (or more) stimuli (Eimer, 2014; McDonald et al., 2009). The addition of this distractor served the dual purpose of reducing sensory refractoriness (i.e., sensory adaptation) through minimising sensory imbalance, as well as allowing for a discrete measure of attentional processes occurring after detection – the posterior-contralateral N2 (N2pc; McDonald et al., 2009; Luck & Hillyard, 1994).

The N2pc is an ERP component originating in the ventral occipito-temporal cortex (Hopf, Vogel, Woodman, Heinze, & Luck, 2002). Its measurement requires simultaneous electrode readings from both cerebral hemispheres (Luck & Hillyard 1994). It is evidenced as a greater negative amplitude in the ERP-waveform from the electrode contralateral to the stimulus being attended over ipsilateral amplitude (see Figure 2; Luck & Hillyard, 1994; McDonald, Hickey, Green, & Whitman, 2009). Peaking between 200-300ms, the amplitude difference between the two hemispheric readings has been demonstrated to index the degree of attention deployed to a

location (McDonald et al., 2009). As such, the measurement of N2pc has often been used as a means by which to monitor the deployment of visuospatial attention (Yang et al., 2012; Maheux & Jolicœur, 2017; Pierce, Crouse, & Green, 2017).

Results of McDonald et al.'s (2009) study showed reduced N2pc amplitudes for cued targets as compared to uncued targets, suggesting an attentional bias against returning to recently attended locations. However, while their justification for the investigation of N2pc modulation in ICEs was sound, and their results suggest that the deployment of attention is inhibited from returning to a recently attended location, their task design did involve oculomotor activation. This observation is important, as current research has suggested that ICEs observed in the absence of oculomotor activation results from sensory processes (e.g., adaptation), with output-based inhibition only observed when it is present (Hilchey et al., 2014). Therefore, whilst the modulation of attentional deployment (N2pc) observed in McDonald et al. (2009) provides encouraging support for the component's use as an electrophysiological marker of inhibition, it has not yet been shown to reflect the

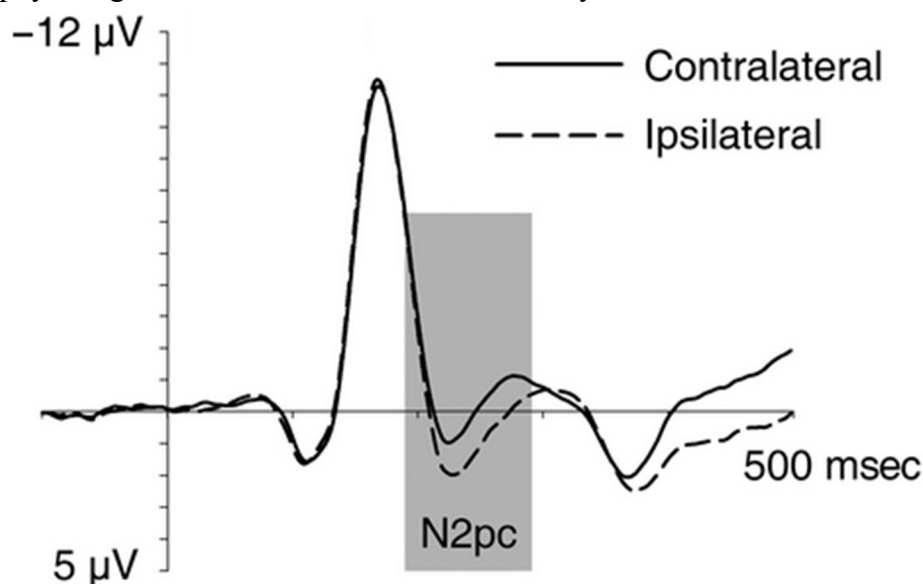


Figure 2. An example of N2 waveforms (contralateral, ipsilateral), with the difference representing the N2pc (Grubert & Eimer, 2015)

mechanism of direct inhibition proposed to generate output-based ICEs.

Attentional Deficits

Given the fact that we, as a species, rely heavily on visual search in almost every aspect of day-to-day life, the identification of a reliable marker of an attentional mechanism underpinning its function can help to provide insight into the way we view the world. Moreover, such a marker has the potential to serve as a research tool in examining the way in which attentional deficits impact upon its function.

A disorder that has been shown to result in such deficits is Attention Deficit Hyperactivity Disorder (ADHD), a neurodevelopmental disorder resulting in compromised attentional capacities (Hasler et al., 2016). This disorder is typically observed in childhood; however, it often persists into adulthood (Cross-Villasana et al., 2015). Due to changes in symptom expression from childhood to adulthood, the diagnosis of ADHD in the latter can prove challenging (Davidson, 2008). It has been shown that, while the experience of hyperactivity symptomology decreases with age, the inattentive components persist (Franke et al., 2018). This can result in negative outcomes for adults with ADHD, impacting on everyday functioning (Franke et al., 2018). Worryingly, research has demonstrated that, of the estimated 2.3-4.5% of the adult population with ADHD, approximately only one third are appropriately diagnosed (Asherson et al., 2012), with some estimates of underdiagnosis higher outside of the United States of America (Asherson et al., 2012).

Relevant to the study of ICEs, individuals with ADHD have been demonstrated to have generally slower behavioural RTs when compared to control groups in tasks of attention (Cross-Villasana et al., 2015). In the context of research into ICEs, this pattern of findings, coupled with high rates of undiagnosed

individuals, suggests that sampling methods that do not control for undiagnosed attentional deficits may risk confounding results.

It has been proposed that the neurological components underlying the findings of slower RTs in ADHD cohorts reflect an impairment of inhibitory processes related to visual search (Cross-Villasana et al., 2015). As both input and output-based ICEs are thought to be influenced by attentional processes, it is conceivable that individuals with attentional deficits, such as those seen in ADHD populations, might display a reduction in observed ICEs within a spatial cueing task (uncued-cued RTs). Although there is limited literature on the influence of attentional deficits on inhibition in spatial cueing, a study by Fillmore, Milich, and Lorch (2009) found that at long CTOAs (1150ms) ICEs found in a control group were not present in a sample of 9-12-year-olds diagnosed with ADHD.

If this observed pattern of results is an accurate reflection of attentional deficits diminishing ICEs, the identification of an electrophysiological marker indexing this reduction has the potential to inform our current understanding of disorders relating to attention, and perhaps even serve to supplement current diagnostic methods.

Study Rationale & Aims

Past research examining a potential neural marker of ICEs has shown inconsistent findings. As such, a reliable neural marker has yet to be identified. Current literature suggests that, while often discussed as being the same, a neural dissociation between input and output-based mechanisms driving ICEs exists that is dependent upon the activation state of the oculomotor system. Based on the evidence for such a dissociation, the present study aims to study previously a proposed electrophysiological marker of the ICE phenomenon when the oculomotor system is

suppressed, and when it is active. Also relevant to the aims of the present study is the way in which attentional deficits (such as those seen in ADHD) impact the effectiveness of inhibitory mechanisms of visual search (i.e., those underlying ICEs). In doing so, the present study aims to replicate the findings of Satel et al. (2013) in observing a main effect of cueing on RT (i.e., ICEs), and in observing greater inhibition when the oculomotor system is activated. Further, the present study seeks to re-examine the modulation of the N2pc component (as in McDonald et al., 2009) while dissociating input and output-based ICEs.

Hypotheses

In line with the findings of Satel et al. (2013), it is hypothesised that there will be a main effect of cueing on RT, such that overall RTs will be slower for cued trials compared to uncued (i.e., ICEs will be observed). It is further hypothesised that the magnitude of inhibition (uncued-cued) will be greater in active-state trials compared in suppressed-state (i.e., greater inhibition in active-state condition). Lastly, it is hypothesised that there will be no main effect of group, but that a group by cueing interaction will be observed, with the overall difference between uncued-cued RTs reflecting diminished ICEs in those with attentional deficits compared to controls. This reduction in inhibition is expected to be greater when the oculomotor system is active.

In line with research implicating oculomotor activation in generating output-based ICEs, and their modulation of attentional processes, it is hypothesised that N2pc amplitude be reduced for cued targets only in the active state. While there is no expected difference in N2pc amplitude in the suppressed state, the reduction expected in the active state is predicted to result in an overall effect of cueing.

Further, it is hypothesised that, overall, there will be reduced amplitude in the active-state condition compared the suppressed-state condition (reflecting inhibited deployment of spatial attention). While there is no expected N2pc modulation in the suppressed state, N2pc modulation in active, along with the proposed impairment of ICEs in those with attentional deficits, is predicted to result in an effect of group. As such, it is hypothesised that, overall, N2pc amplitude will be reduced in the deficit condition. This reduction is hypothesised to be of lesser magnitude for those with attentional deficits (evidenced as an Oculomotor-State by Group interaction)

Method

Participants

An a-priori power analysis indicated that, for the detection of a moderate effect ($f = .25$), at a power of 0.8, a sample of 29 participants was sufficient. To compensate for incomplete or unusable data (e.g., noisy EEG traces) the present study recruited a sample of 40 participants (25 Females) aged between 18 and 47 years (*Mean age* = 25.00, *SD* = 8.07) via word of mouth and by way of the University's online research participation system (SONA). Seven participants were excluded from analyses due to excessive artefacts in the EEG traces, resulting in an insufficient number of completed trials. Thus, the final sample comprised of 33 participants (20 Females), aged between 18 and 47 years of age (*Mean age* = 24.82, *SD* = 8.39).

Participants were compensated for their time with either two hours research credit (eligible students), or a cash payment (\$15 per hour). To be eligible for participation in this study, it was a requirement for participants to be ≥ 18 years of age, to have normal (or corrected-to-normal) vision, and no existing psychiatric or neurological disorders.

Design

The present study employed a 2 x 2 x 2 mixed factorial design, with separate analyses conducted for each dependent variable. Within groups factors were Oculomotor-State (Active, Supressed) and Cueing (cued, uncued), the between groups factor was Group (control, attentional deficits). The dependent variables were manual response time (RT; ms) and N2pc amplitude (μ V).

Materials

Eye tracking. High-precision eye-tracking hardware and software was used in order to monitor the eye position of participants throughout both conditions to ensure no eye-movement in the suppressed state (desktop mounted EyeLink 1000 Plus system from SR Research, 500Hz).

Electroencephalography. A 32-channel EEG system (250Hz, ActiChamp gel-based system from Brain Products) was used to record ongoing neural activity from which ERP components were extracted. EEG recording was referenced to FCz during acquisition, with a high-pass filter of 1Hz, and a low-pass filter of 30Hz. All target epochs from -100ms to 400ms were extracted, with a baseline correction of 100ms (-100ms to 0ms). Any epoch with a ± 75 microvolt deflection in the time window were considered artefacts and removed.

N2pc amplitude was extracted by finding the most positive time-point in the contralateral-ipsilateral difference wave in parietal electrodes (P7/8) between 250-350ms and taking an average of 80ms centred around this point.

Spatial Cueing Task. Participants completed a modified spatial cueing task (see Figure 2), administered with MatLab on a 27" monitor connected to an Intel Corei7-6700 (3.40GHz) processor.

In this task a black screen was presented with a circle (measuring $.8^\circ$ degrees of visual angle) which served as a point of fixation between trials (inter-trial interval; ITI). Once a trial had begun, the circle disappeared and three separate boxes (each measuring $4.5^\circ \times 4.5^\circ$ of visual angle) with white borders measuring one pixel, equally spaced in a horizontal manner, were presented. The centre box signified the point at which participants would fixate. The distance between the edge of the fixation box and the edge the boxes flanking it was distanced at 8.7° of visual angle. This is the fixation period, following which a cue was presented for 200ms. The cue stage of a trial entailed the borders of one of the flanking boxes increasing in width from one to 10 pixels – this occurrence was equiprobable (i.e., 50/50, or chance frequency). Following this, an inter-stimulus interval (ISI) of 1300ms occurred, the screen presented during this phase is identical to the fixation screen occurring at the beginning of the trial. Following the ITI a target was presented, again equiprobably (with a diameter of 2.4°). Concurrent to the target, a distractor, equal in size and similar in structure, was presented in the square opposite. The two stimuli (x, +) were counterbalanced, with the target indicated to participant as the red stimulus (i.e., the target [x or +] was always red). The target presentation phase lasted until a manual response was recorded, or until a period of 3000ms had elapsed. Finally, an ITI screen was presented for a randomised duration of time between 750ms and 1250ms. This completed the time-course of a trial.

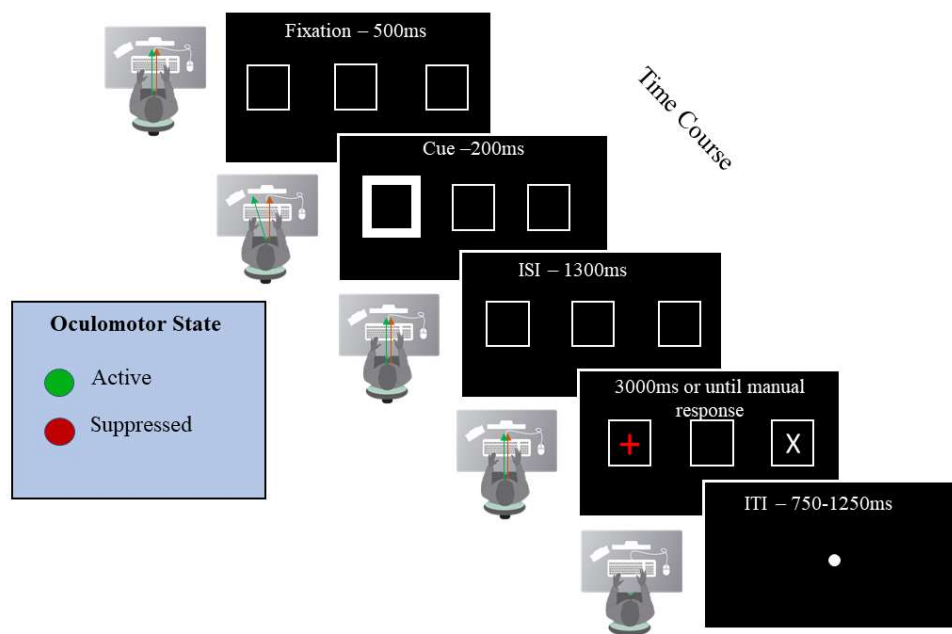


Figure 3. Time-course of a cued target trial in the spatial cueing task employed in present study.

Attentional Questionnaire. In order to screen for attentional deficits, the Adult ADHD Self-Report Scale Symptom Checklist (ASRS v1.1; Appendix A) was administered prior to participation. The ASRS, and its scoring system, is a reliable and valid (Adler et al., 2006) self-assessment of ADHD symptoms in adults developed by a World Health Organisation workgroup (Kessler et al., 2005). The scale consists of 18 items corresponding directly to DSM-IV symptoms of ADHD. The items are split into part A and part B (9 questions each) and are rated on a 5-point likert scale (never, rarely, sometimes, often, and very often). Scores for each section are summed, If the score is less than 17 it is considered unlikely that the participant has ADHD, between 17-23 it is likely, and greater than 24 it is extremely likely. If the participant scores 17 or above, they are seen as having symptoms consistent with ADHD (Kessler et al., 2005).

Procedure

The undertaking of this study was approved by the Tasmania Human Research Ethics Committee (Appendix B) prior to commencement of participant

recruitment. Participants were provided an information sheet (see Appendix C) and were also given a verbal explanation of the purpose of the study, what the task entailed, as well as the apparatus that would be used. Following this, informed consent was obtained in writing (see Appendix D). Participants were then asked to fill out the ASRS, linked to their experimental data and separated from their personal information by way of a numerical identifier; in this way the data was de-identified. Once consent had been obtained and the ASRS completed, participants were seated, and the EEG electrode cap was fitted. To ensure that the cap was correctly positioned, measurements were taken against a reference point on the cap. Lateral measurements were taken from the top-most point of one ear to the other, posterior-anterior measurements were taking from the bottom of the frontal bone to the occipital bone. Satisfactory electrode connections were established via the application of electrolyte gel (no impedances above 50m Ω).

Participants were then positioned, in a light-controlled room, with their eyes at a distance of 60cm from the screen, and the eye-tracking hardware and software were calibrated (5-point calibration procedure). Participants then completed 24 practice trials (12 active, 12 suppressed) before commencing the experimental conditions (400 trials). In completing a trial, participants were instructed to maintain their gaze within the point of fixation unless otherwise instructed. Within this task there were two conditions, with separate instructions, diverging at the point of cue onset. In one, participants were asked to move their eyes to the cue and then back to fixation prior to target onset (active), and another in which they were asked to remain fixated throughout trials (suppressed). The order of these conditions was counterbalanced across participants such that half would complete the active condition first and move on to the suppressed condition and vice versa. In the active

condition, when participants were required to make a saccade, this eye movement was required to be accurate within 3° of visual angle. When a saccade was made that was outside of this angle, or when gaze did not reach the target or return to fixation prior to 600ms, the eye-movement was considered to be inaccurate. In such an instance, the trial was terminated, an error message was displayed, and the trial was recycled randomly to be completed again. Upon presentation of the target, participants were required to make a manual localisation response in the form of a keypress corresponding to the location of the target – left or right (“z” [left], “/” [right]).

Analysis

Data was assessed to ensure that the assumptions of ANOVA had been met. Individual RTs greater than 2.5 units above/below the median absolute deviation¹ were considered outliers (anticipatory or excessively delayed) and subsequently excluded from the analysis. Out of completed trials, 10.7% were removed for being delayed and 2.2% were removed for being anticipatory. Additionally, 1% of trials were excluded due to excessive noise. In total, 86.2% of completed trials were considered appropriate for analysis.

The data of participants scoring above 17 on the ASRS were placed in the deficit level of Group (11). Equally, those scoring below 17 were placed in the control level (22).

The behavioural dependent variable for the spatial cueing task was manual RT (ms). This was analysed using a 2 (Group: control, deficit) x 2 (Cueing: cued, uncued) x 2 (Oculomotor-State: active, suppressed) repeated measures ANOVA.

¹ The use of a moderately conservative (2.5) median absolute deviation exclusion criteria was justified as it has been shown to be a more robust measure of the variability of a sample in the presence of outliers than the mean \pm three standard deviation method (see Leys, Ley, Klein, Bernard, & Licata, 2013)

Post-hoc pairwise comparisons (with family-wise error rate adjustments) were conducted where appropriate.

The electrophysiological dependent variable was peak amplitude of the N2pc mean-difference component in the ERP waveform. Analysis of N2pc amplitude was undertaken using a 2 (Group: control, deficit) x 2 (Cueing: cued, uncued) x 2 (Oculomotor-State: active, suppressed) repeated-measures ANOVA.

Results

Behavioural Results

Results of a 2x2x2 repeated-measures ANOVA examining the effect of Cueing, Oculomotor activation, and Group on behavioural RT (ms) revealed a main effect of Cueing $F(1, 32) = 28.24, p < .001, \eta_p^2 = .48$, such that RTs (ms) to cued targets were significantly slower ($M = 359.14, SD = 46.30$) than uncued ($M = 345.20, SD = 38.91$) in both the active-state ($MDiff = 13.96, 95\% CI [8.51, 19.41]$) and suppressed-state ($MDiff = 13.68, 95\% CI [8.73, 18.63]$) conditions (i.e., ICEs were observed; see Figure 3.). Results of the same ANOVA showed no main effect of Oculomotor-State $F(1, 31) = .005, p = .947, \eta_p^2 = .00$ or Group $F(1, 32) = .09, p = .767, \eta_p^2 = .00$.

No interaction of Group and Cueing was observed $F(1, 31) = 3.16, p = .086, \eta_p^2 = .09$, however there was a trend toward significance. Due to this near significance, the moderate effect size observed, and the hypothesised pattern of reduced inhibition for participants with attentional deficits, tests of simple main effects were conducted with Bonferroni adjusted alpha ($\alpha = .025$). Pair-wise comparisons revealed a significant ($p < .001, g = .27$) effect of cueing in the control group, such that RTs (ms) to cued targets were significantly slower ($M = 361.68, SD = 49.34$) than those to uncued targets ($M = 345.07, SD = 39.39$). However, this difference was not observed in the deficit group, with responses to cued targets not significantly differing from

those to uncued ($p = .040$, $g = .19$). However, there was a trend toward significance, showing slower RTs in cued ($M = 352.91$, $SD = 36.88$) than uncued ($M = 344.68$, $SD = 33.81$) trials.

No interaction was observed between Cueing and Oculomotor-State $F(1,31) = .01$, $p = .912$, $\eta_p^2 = .00$, or Group and Oculomotor-State $F(1, 31) = .47$, $p = .497$, $\eta_p^2 = .02$. No interaction of Group, Cueing, and Oculomotor-State was observed $F(1,31) = .01$, $p = .932$, $\eta_p^2 = .00$.

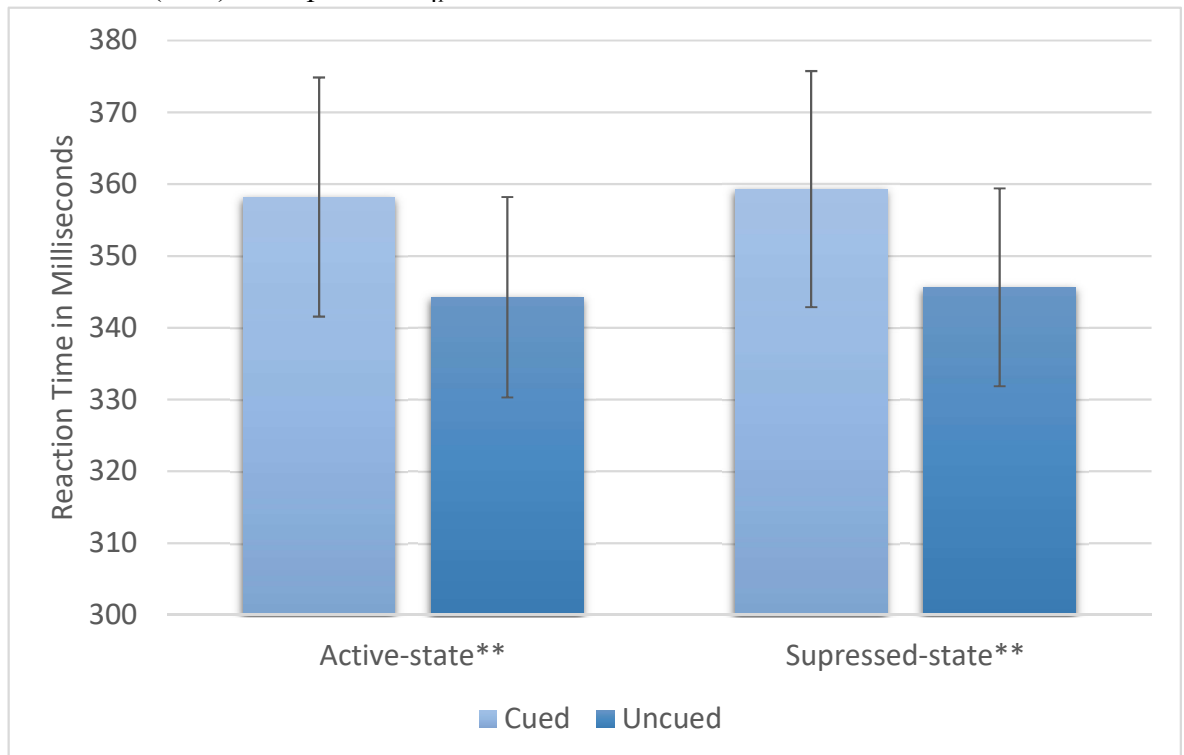


Figure 4. Means and 95% confidence intervals for the effect of Cueing on RT. [** $p < .001$]

N2pc Results

Results of a 2x2x2 repeated-measures ANOVA examining the effect of Cueing, Oculomotor activation, and Group on N2pc difference-wave amplitude (μV) revealed no main effect of Cueing, Oculomotor-State, or Group, $F(1,31) = 1.99$, $p = .169$, $\eta_p^2 = .06$, $F(1,31) = .03$, $p = .863$, $\eta_p^2 = .00$, $F(1,31) = .632$, $p = .433$, $\eta_p^2 = .20$, respectively.

Results of the same ANOVA revealed no interaction of Cueing and Group, Oculomotor-State and Group, or Cueing and Oculomotor-State, $F(1,31)=.62$, $p=.436$, $\eta^2=.02$, $F(1,31)=.95$, $p=.337$, $\eta^2=.03$, $F(1,31)=.49$, $p=.488$, $\eta^2=.02$, respectively. Further, no three way interaction was observed for Cueing, Oculomotor-State, and Group $F(1,31)=1.18$, $p=.287$, $\eta^2=.04$ (see figures 5-8 for grand average waveforms).

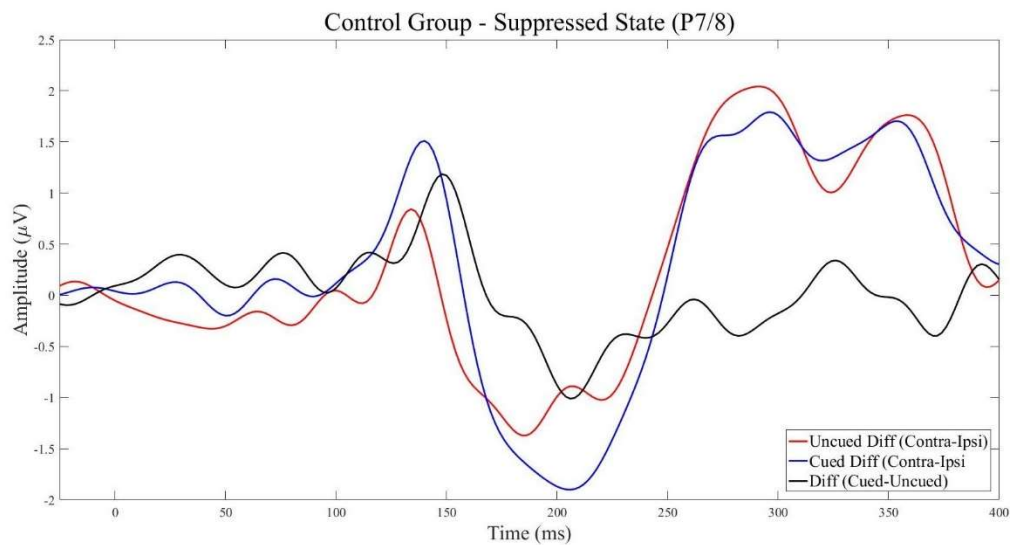


Figure 5. Grand average waveforms for control group with active oculomotor state

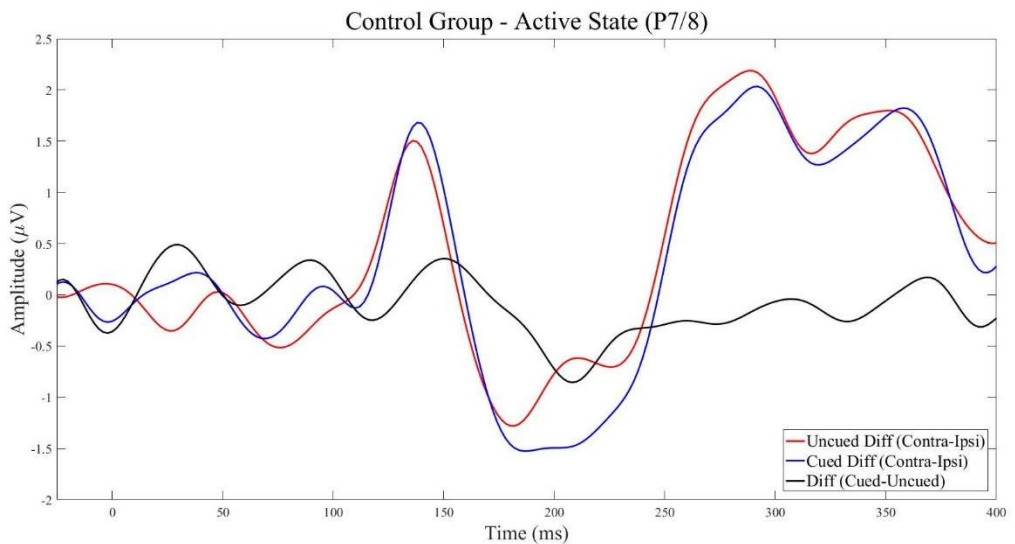


Figure 6. Grand average waveforms for control group with suppressed oculomotor state

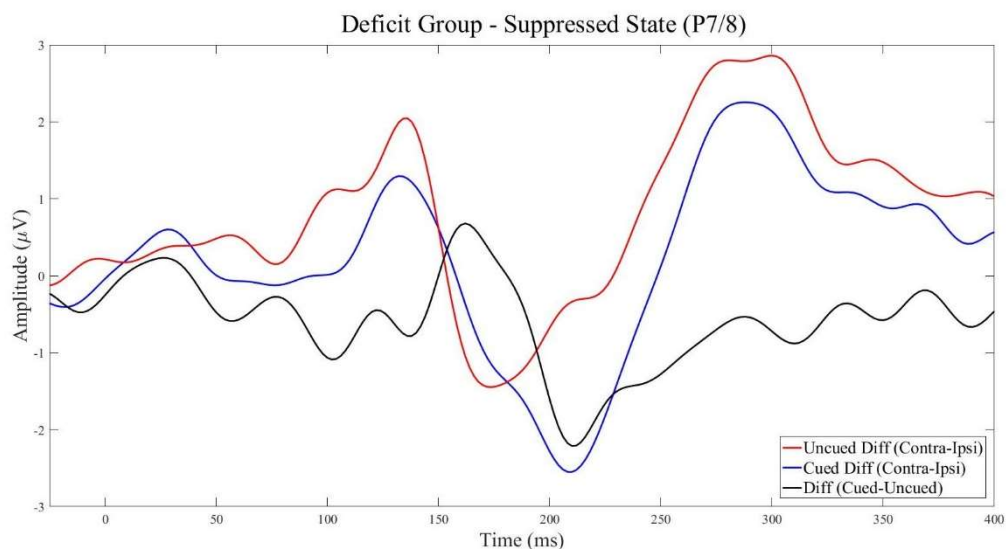


Figure 7. Grand average waveforms for deficit group with active oculomotor state

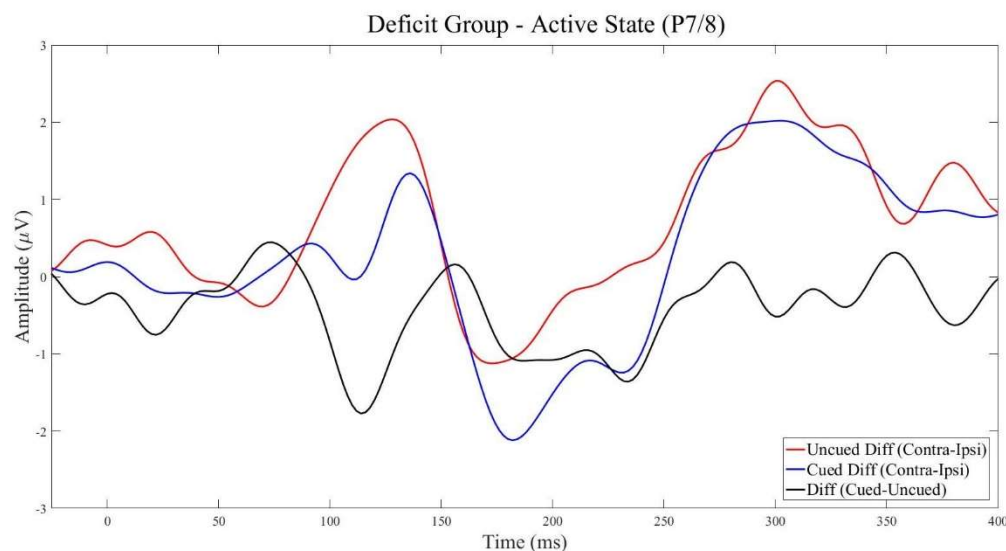


Figure 8. Grand average waveforms for control group with active oculomotor state

Discussion

Behavioural

Results of the present study supported the prediction that overall RTs would be slower for cued targets than for uncued targets. These findings are consistent with the findings of previous literature demonstrating observable inhibition to targets preceded by un-informative cues in tasks of spatial cueing (Satel et al., 2013; Hilchey

et al., 2014; Klein, 2000). Such findings confirm that the spatial cueing task used in the present study elicited ICEs.

The prediction that greater inhibition (slower RT to cued>uncued) would be observed when the oculomotor system was active was not supported. This was evidenced by a non-significant interaction. Inspection of means, standard deviations, and 95% confidence intervals support this conclusion, showing cued and uncued RTs, as well as RT difference (uncued-cued; inhibition) in the active state condition to be statistically indistinguishable from those in the suppressed state condition. Such a finding is contradictory to that of a recent study which used a target-distractor spatial cueing design (Eng, Lim, Janssen, & Satel, 2018). Using a design similar to that of the current study, Eng et al. (2018) found significant ICEs to peripherally cued targets at a CTOA of 1600ms when the oculomotor system was active. One notable difference between their study and the current one was that the target and distractor were both white (while in the present study the target was always red).

This observation may be of importance, in that the colour red has been shown to function, in humans and primates, as a signal of threat (Elliot & Aarts, 2011; Setchel & Wickings, 2005). In the context of visual attention, threatening stimuli have been shown to automatically capture attention (Schmidt, Belopolsky, & Theeuwes, 2012). It is thought that the processing of threatening stimuli involves the amygdala (a subcortical structure implicated in detection of danger) and occurs via two pathways – cortical (slow) and subcortical (fast; Schmidt et al., 2012). It is this subcortical route that is proposed to involve the SC and result in the generation of activity within the oculomotor system (Schmidt et al., 2012). Thus, it is within the realm of possibility that the red target used in the current study was implicitly perceived as a threatening stimulus and processed via this subcortical route. If this

were the case, then the resultant activity generated within the oculomotor system may have invalidated the suppressed-state condition. This interpretation is in line with the findings of Rafal et al. (1989) who demonstrated that a condition requiring a participant to merely prepare a saccade is sufficient to result in inhibition of equal magnitude to one in which a saccade was completed. In such an instance, the suppressed-state condition of the current study would be analogous to the planned saccade condition of Rafal et al (1989) and would not reflect a truly suppressed oculomotor system. This interpretation accounts for the finding similar ICEs across the two levels of Oculomotor-State (i.e., because both conditions were active), and for the non-significant main effect of Oculomotor-State.

The findings of the present study supported the hypothesis that there would be no overall difference in RTs between groups. This was confirmed by the absence of a significant main effect of group showing the combined RTs (uncued, cued) of the control group to not statistically differ from those of the deficit group.

One possible explanation of this lies in the consistent observation of the slower RTs in the ADHD population when completing tasks of attention. Due to this, one would expect that combined RTs for an ADHD cohort would be significantly slower than those of a control. However, as discussed previously, the study of ICEs involves the study of inhibitory processes – processes that have been shown to be potentially impaired in those with attentional deficits. Such an impairment of the inhibitory process(es) underlying ICEs would result in faster RTs to cued targets (i.e., responses are less inhibited), thereby mitigating the effect of overall slower responses.

Further, results supported the prediction that the overall difference between uncued-cued RTs would be significantly lessened in the deficit condition. While the

Cueing by Group interaction was only marginally significant, post-hoc pairwise comparisons (justified by moderate effect size and theoretical relevance) with family-wise error adjustments were conducted. These comparisons revealed a significant difference in the control group, indicating that ICEs had been observed. In contrast, comparison of the cueing effect in the deficit group showed RTs for uncued and cued trials to be statistically equivalent. However, the significance of the uncued-cued difference in the deficit condition was approaching significance and both the deficit and normal conditions had comparable effect sizes (with overlap of the 95% confidence intervals). This finding suggests the possibility that the difference in the deficit group was significant, and that perhaps the sample size of the condition did not provide sufficient power to observe significance. Inspection of the mean difference (uncued, cued) in both the control and deficit groups show that the inhibition in the latter was halved. If it is the case that a lack of power resulted in a type II error (i.e., there was a significant difference that was not observed), then these findings would be in line with the hypothesis that inhibition within the deficit group would be reduced but still present.

Alternately, if a type II error was not made, such findings would be consistent with the proposal of compromised inhibitory processes in those with attentional deficits in that, in that there was an absence of ICEs. This result is consistent with the findings of Fillmore et al. (2009) suggests that attentional deficits of this degree are sufficient to counteract, entirely, a robust inhibitory process. This finding is a potentially important one, in that it raises the possibility of quantifiable measure of compromised inhibitory processes (such as those seen in ADHD). Given that the diagnosis of such disorders is based predominantly on behavioural observations from clinical interviews and the administration of symptom rating scales (Rösler et al.,

2006), the identification of such a measure could serve to improve the accuracy of diagnoses. However, the present study did not control for comorbidities, nor use a population with a clinically diagnosed attentional disorder. Together with the small sample size of the deficit group (relative to control), these findings demand further and more in-depth examination in order to clarify extent to which attentional deficits influence ICEs.

The hypothesis that the reduction in inhibition would be larger in the active state than the suppressed state was not supported. This finding is reflected in the non-significant three-way interaction and is consistent with the interpretation that both Oculomotor-State conditions were, in fact, active.

Electrophysiological

Results of the present study did not support the hypothesis that N2pc would be elicited, and that an overall reduction in the amplitude of the mean difference wave would be observed between uncued and cued trials. This is evidenced as a non-significant main effect of cueing in the repeated-measures ANOVA. In interpreting this finding, it is important to note that, in place of the expected N2pc, an ERP component was observed with similar latency and topographical properties, but with a positive polarity (see Figures 5-8)

A possible explanation of this finding comes from the contingent involuntary orienting hypothesis (CIOH), a theory proposing that involuntary shift of attention to stimuli are contingent on whether they share a critical property with a target (i.e., a property relevant to task performance; Folk, Remington, & Johnston, 1992). If the stimulus does not share such a property, then involuntary orienting of attention will not occur. The CIOH posits that, in such instances, attentional capture will be less a consequence of bottom-up (salience driven) processing, and more so to do with

current top-down (or goal driven) processes and so involuntary capture will be less likely (Mertes, Wascher, & Schneider, 2016). Findings of studies examining this effect have, however, shown inconsistent results (Mertes et al., 2016).

Building on the notion of contingent orienting, Kiss, Grubert, Peterson, and Eimer (2012) proposed that variation in temporal task demands on attentional capture play a critical role in processes underlying attentional capture. Using the N2pc ERP component, they examined the deployment of attention to visual search targets in the presence of a distractor under high temporal demand (participants had to respond within a short time-frame) and low demand (no time constraints). They found that, when there was a high temporal demand, instead of the distractor eliciting an N2pc (indicating attentional capture) a positive contralateral-ipsilateral difference (or Pd) was observed when a lateral target was presented with a lateral distractor in the opposite hemisphere (Kiss et al., 2012). This Pd was interpreted as reflecting a top-down inhibition of attentional capture (Kiss et al., 2012), and is consistent with the findings of McDonald et al. (2009), who found that, in the presence of a distractor, when participants asked to merely detect the presence of a target, the Pd was eliminated. This absence suggests that the suppression of distractors is only occurring when attentional demands of the task are high (McDonald et al., 2009; Kiss et al., 2012). Due to the attentional demands and time constraints of the task used, the findings of Kiss et al. (2012) suggest that their observation of a Pd indicates the presence of a mechanism actively suppressing attention shifts to distractors.

The present study found an inverse polarity akin to that observed in Kiss et al. (2012) across uncued and cued conditions, with a large positive contralateral inflection and smaller positive ipsilateral inflection. Considering the CIOH and the findings of Kiss et al. (2012) and McDonald et al. (2009), it is possible that the

instruction to participants to respond as quickly as possible placed a high temporal demand on their completing the task. Given that such demands have been shown to result in a process of distractor suppression, this is a plausible explanation for why the N2pc component was not observed. Put simply, the process of distractor suppression is top-down, driven by an implied strategy. As participants knew that the target would be red it appears that, as part of a cognitive strategy adopted in response to task demands, automatically suppressed stimuli of any other colour (i.e., the white distractor), thus generating a Pd.

A drawback to the Pd explanation, however, is that whereas, in the current study, the positive difference observed is contralateral to the target, Pd is typically characterised as positivity contralateral to the distractor (Gaspar et al., 2016; Burra & Kerzel, 2014; but see Sawaka, Geng, & Luck, 2012 for evidence of a Pd contralateral to target). An alternate explanation for this finding is that in place of an N2pc or Pd, the contralateral positivity observed in the ERP-waveforms reflects a contralateral-ipsilateral temporal positivity (Ptc) - a positivity typically observed contralateral to the target (Hilimire, Mounts, Parks, & Corballis, 2010). Occurring approximately 290-340ms after target onset, the Ptc, much like the Pd, is an ERP component thought to index suppression (Hilimire et al., 2010). Crucially, however, the Ptc is proposed to reflect a mechanism of target suppression, rather than distractor suppression, as a means by which attention is disengaged (Hilimire and Corballis, 2014)

Relevant to the findings of the current study, and interpretation of the unexpected positivity observed, the amplitude of this component has been shown to be increased in response to red stimuli (Pomerleau, Fortier-Gauthier, Corriveau, Dell'Acqua, & Jolicoeur, 2013). Moreover, Pomerleau et al. (2013) found that, when target stimuli

are red (or blue), N2pc components have significantly earlier onset and peak (mean latency of 205ms compared to 250ms for green and 253ms for yellow; Pomerleau et al., 2013). While inspection of the ERP waveforms does not suggest the presence of an N2pc, the current study extracted peak amplitudes between 250ms and 350ms. Given the findings of Pomerleau et al. (2013), and the fact that the experimental design of the present study used a red target, it is possible that this window was at too late a time-point to detect an N2pc, or that the increased amplitude in response to the red target was masking it (or a combination of the two). This explanation is consistent with the theoretical conceptualisation and typical latency of the Ptc component, in that it is typically observed at time-points subsequent to N2pc and has been proposed to reflect a mechanism by which deployed attention (reflected by N2pc) is disengaged (Hilimire et al., 2010). Taken together, the evidence supports this interpretation as the most likely, and theoretically justifiable, explanation of the observed positivity.

Findings did not support the prediction of a greater negative amplitude of the N2pc mean difference wave in the oculomotor condition, with a non-significant main effect of Oculomotor-State indicating that amplitude was observed to be equal across both active and suppressed states. While this finding is contrary to the prediction of the study, it is consistent with the notion that the suppressed-state condition of the task did not entirely suppress oculomotor activity. That is, as discussed previously, if there was oculomotor activity when the oculomotor system was supposed to be suppressed, then the mechanism of inhibition proposed to generate greater inhibition in an active state would be present in both levels of the condition. The presence of this inhibition in both conditions would mean that present study would not be able to observe the hypothesised modulation through dissociating suppressed and active

states as all trials were, in fact, active. This interpretation also accounts for the finding that the hypothesised interaction of Oculomotor-State by Cueing was non-significant.

Results did not support the hypothesis of a reduced negative amplitude of the N2pc mean difference wave in the deficit group, as evidenced by a non-significant main effect of group in the repeated-measures ANOVA. This can be attributed to the fact that the positive difference in the waveform observed is not reflective of attentional deployment so much as a suppression/disengagement of attentional capture (Hillmire and Corballis, 2014). Therefore, examination of this ERPs modulation across Oculomotor-State would not provide an index of attention, so much as one of attentional disengagement. This interpretation is consistent with the findings of the present study which show no difference between control and deficit groups (i.e., equal positive amplitudes).

If the positivity observed was, indeed, a Ptc, a possible explanation of the similarity observed across groups can be found in studies examining the persistence of attentional deficits across the lifespan. In a recent study of this nature, Stigchel, Hessels, van Elst, and Kemner (2017) found that the difference in capacity to effectively disengage attention between those with ADHD and a normal population decreases with age. Because the attentional deficit cohort used in the present study comprised entirely of adults, it is likely that attentional disengagement of this group was comparable to that of the control – thus elucidating the finding of equivalent Ptc amplitudes.

The hypothesised interaction of Oculomotor-State and Group was not supported by the findings of the present study. Again, this can be attributed to the oculomotor activity present in both state conditions.

Limitations

A primary limitation of the present study, and one that has been discussed previously, is the confounding effect of the red target – specifically, its proposed implicit priming of the oculomotor system. In generating activity within the oculomotor system, the red target potentially invalidated the suppressed level of Oculomotor-State, thus limiting the ability of the present study to draw conclusions relating to ICEs (and their modulation of N2pc) in the context of a suppressed and active oculomotor system. While, in retrospect the use of the colour red to signify the target appears to have been a methodological oversight, a distinct lack of literature on the effects of colour on ICE generation means that it was one that proved difficult to foresee. If the theorised effect of the red stimulus on oculomotor activation proves to be correct, this suggests that additional steps, beyond those taken in the present study (i.e., eye-tracking) should be taken to ensure the suppression of the oculomotor system in future research.

A further limitation of the present study was the absence of P07/08 electrode sites on the EEG caps used. These sites are more posterior and slightly more medial than the P7/P8 electrodes used in the present study. Specific to the explanation of Ptc being observed in place of N2pc, these electrode sites are acknowledged to be the region at which amplitude of the latter is maximal (Eimer & Kiss, 2007). This becomes a limitation as the Ptc, as its name implies, is stronger at more lateral-posterior electrode sites (Hilimire, 2010). In contrast, while the N2pc is still observable at posterior-lateral sites, the amplitude of Ptc is maximal at these sites (in particular P7/P8; Hilimire & Corballis, 2014). When considered in combination with the likelihood of an early-onset N2pc, increased Ptc amplitude (due to the red target),

the use of electrode sites where the Ptc is maximal, and the N2pc is not, may have impeded the ability of the present study to examine the deployment of attention.

Future Directions

It is recommended that future research explore the proposition that the red target resulted in a threat response (and subsequent oculomotor activity) through employing a task design similar to that of the present. In investigating this explanation, it is recommended that the task used in the present study be altered so that no saccades are required at all. Additionally, it is recommended that a two-level target-colour condition including both white and red targets be utilised. If oculomotor activity is generated as a response to the red target, such a design would be expected to observe both input and output-based ICEs when it is present. Conversely, when the white target is used, no oculomotor activity would be expected to be present. In line with research demonstrating oculomotor activation, in spatial cueing paradigms, to result in greater inhibition, comparison of uncued-cued inhibition between red and white targets would be expected to show a reduction in the latter.

In clarifying the cause of the observed positivity, it is recommended that future research use a similar design as outlined above. In this way, the role of the red stimulus on ERP latency can be controlled for. If, indeed, the red target resulted in an earlier N2pc, comparison of the waveforms (peak amplitudes, latency) between the red and white targets will allow researchers to clarify the findings of the present study. Based on the findings of Pomerleau et al. (2013), it is expected that the red target will result in the N2pc occurring at an earlier-than-usual time-point, and that the Ptc observed between 250ms-350ms will be replicated. In contrast, when the white target is present, the N2pc is likely to be observed within the usual latency range, with the Ptc occurring subsequent to this. Further, to control for early-onset

N2pc, it is recommended that the measurement of this component in such a design is taken from both an early and late latency range (see Eimer and Kiss, 2007), and that P07/P08 electrode sites are included.

Additionally, the potential absence of ICEs within the attentional deficit level of Group merits further investigation. It is recommended that future research into this finding utilises a clinically diagnosed population, controls for comorbidities, and recruits a sufficient (and equal to control) sample. Methodological flaws within the design of the present study have meant that it was not possible to examine how attentional deficits differentially effect both types of ICEs. In order to allow for such investigation, it is recommended that future research on this topic employ both an active and suppressed oculomotor condition. Due to the proposed attentional mechanism underlying output-based ICEs, it is expected that a design of this nature would observe reduced or absent ICEs when the oculomotor system is active.

Lastly, from a final sample of 33 participants, 11 were found to score highly enough on the ASRS so as to be deemed ‘likely’ as having ADHD. While research has suggested that rates of undiagnosed ADHD in adult populations are typically underestimated, the proportion of those with some level of attentional deficit found in the current sample is surprising. Given the findings of the present study suggest that such deficits have the potential to impair attentional processes, it is recommended that future research investigating ICEs utilise an attentional screener, such as the ASRS, as a means by which to pre-empt potential confounds.

Summary and Conclusions

It was the aim of the present study to expand upon research suggesting a neural dissociation between input and output-based ICEs, and to identify a potential electrophysiological marker of the latter. To achieve this, the modulation of deployed

covert attention (by way of N2pc) was investigated with and without oculomotor activation. Additionally, the present study aimed to examine the extent to which attentional deficits influence the observation of ICEs (as measured by RTs), and modulate N2pc amplitude, across both active and suppressed oculomotor-states.

Results of the present study showed, as was expected, ICEs were elicited across both Oculomotor-State conditions. The inhibition, however, was found to be of equal magnitude, with RTs in the two conditions statistically indistinguishable. As discussed previously, this is likely attributable to the unintended activation of the oculomotor system resulting in output-based ICEs being elicited in both conditions.

While ICEs were observed overall, post-hoc analysis revealed that inhibition (uncued-cued) in the deficit group did not reach significance, however a trend toward slower RTs to cued targets was observed. No modulation of the N2pc component was observed, with similar amplitude across levels of all conditions. However, a polarity inverse to that expected was identified at the time-point at which an N2pc was anticipated, suggesting the observation of a Pd or Ptc component.

The confounding effect of the red target, resulting in the activation of the oculomotor system in both active and suppressed states, is proposed to explain the identical inhibition observed across the two conditions. In relation to the aims of the present study, this meant that modulation of ERPs across input and output-based ICEs, within and between attentional groups, was not able to be examined. The proposal that a red target within a spatial cueing task results in oculomotor activation is a novel one, and one that, if confirmed, would have implications on the task design of future research.

The finding of a non-significant cueing effect in the deficit group is an interesting one that merits further investigation in a clinical sample. If replicated, the

absence of ICEs in those with attentional deficits will serve to better inform our understanding of attentional disorders, and, if found to be reliable, may even prove useful in supplementing clinical diagnoses.

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Appendix A

Adult Self-Report Scale (ASRS)

Adult Self-Report Scale (ASRS) Symptom Checklist

Participant Number	Today's Date					
<p>Please answer the questions below, rating yourself on each of the criteria shown using the scale on the right side of the page. As you answer each question, circle the correct number that best describes how you have felt and conducted yourself over the past 6 months. Please give this completed checklist to your healthcare professional to discuss during today's appointment.</p>						
	Never	Rarely	Sometimes	Often	Very Often	Score
1. How often do you make careless mistakes when you have to work on a boring or difficult project?	0	1	2	3	4	
2. How often do you have difficulty keeping your attention when you are doing boring or repetitive work?	0	1	2	3	4	
3. How often do you have difficulty concentrating on what people say to you, even when they are speaking to you directly?	0	1	2	3	4	
4. How often do you have trouble wrapping up the final details of a project, once the challenging parts have been done?	0	1	2	3	4	
5. How often do you have difficulty getting things in order when you have to do a task that requires organization?	0	1	2	3	4	
6. When you have a task that requires a lot of thought, how often do you avoid or delay getting started?	0	1	2	3	4	
7. How often do you misplace or have difficulty finding things at home or at work?	0	1	2	3	4	
8. How often are you distracted by activity or noise around you?	0	1	2	3	4	
9. How often do you have problems remembering appointments or obligations?	0	1	2	3	4	
Part A – Total						
10. How often do you fidget or squirm with your hands or feet when you have to sit down for a long time?	0	1	2	3	4	
11. How often do you leave your seat in meetings or other situations in which you are expected to remain seated?	0	1	2	3	4	
12. How often do you feel restless or fidgety?	0	1	2	3	4	
13. How often do you have difficulty unwinding and relaxing when you have time to yourself?	0	1	2	3	4	
14. How often do you feel overly active and compelled to do things, like you were driven by a motor?	0	1	2	3	4	

15. How often do you find yourself talking too much when you are in social situations?	0	1	2	3	4	
16. When you're in a conversation, how often do you find yourself finishing the sentences of the people you are talking to, before they can finish them themselves?	0	1	2	3	4	
17. How often do you have difficulty waiting your turn in situations when turn taking is required?	0	1	2	3	4	
18. How often do you interrupt others when they are busy?	0	1	2	3	4	
Part B – Total						

Appendix B

Ethics Approval Letter

Social Science Ethics Officer
Private Bag 01 Hobart
Tasmania 7001 Australia
Tel: (03) 6226 2763
Fax: (03) 6226 7148
Katherine.Shaw@utas.edu.au



HUMAN RESEARCH ETHICS COMMITTEE (TASMANIA) NETWORK

26 September 2017

Dr Jason Satel
Psychology
University of Tasmania

Sent via email

Dear Dr Satel

Re: MINIMAL RISK ETHICS APPLICATION APPROVAL
Ethics Ref: H0016857 - Investigating neural mechanisms of visual attention with eye tracking technology

We are pleased to advise that acting on a mandate from the Tasmania Social Sciences HREC, the Chair of the committee considered and approved the above project on 26 September 2017.

This approval constitutes ethical clearance by the Tasmania Social Sciences Human Research Ethics Committee. The decision and authority to commence the associated research may be dependent on factors beyond the remit of the ethics review process. For example, your research may need ethics clearance from other organisations or review by your research governance coordinator or Head of Department. It is your responsibility to find out if the approval of other bodies or authorities is required. It is recommended that the proposed research should not commence until you have satisfied these requirements.

Please note that this approval is for four years and is conditional upon receipt of an annual Progress Report. Ethics approval for this project will lapse if a Progress Report is not submitted.

The following conditions apply to this approval. Failure to abide by these conditions may result in suspension or discontinuation of approval.

1. It is the responsibility of the Chief Investigator to ensure that all investigators are aware of the terms of approval, to ensure the project is conducted as approved by the Ethics Committee, and to notify the Committee if any investigators are added to, or cease involvement with, the project.

A PARTNERSHIP PROGRAM IN CONJUNCTION WITH THE DEPARTMENT OF HEALTH AND HUMAN SERVICES

2. Complaints: If any complaints are received or ethical issues arise during the course of the project, investigators should advise the Executive Officer of the Ethics Committee on 03 6226 7479 or human.ethics@utas.edu.au.
3. Incidents or adverse effects: Investigators should notify the Ethics Committee immediately of any serious or unexpected adverse effects on participants or unforeseen events affecting the ethical acceptability of the project.
4. Amendments to Project: Modifications to the project must not proceed until approval is obtained from the Ethics Committee. Please submit an Amendment Form (available on our website) to notify the Ethics Committee of the proposed modifications.
5. Annual Report: Continued approval for this project is dependent on the submission of a Progress Report by the anniversary date of your approval. You will be sent a courtesy reminder closer to this date. **Failure to submit a Progress Report will mean that ethics approval for this project will lapse.**
6. Final Report: A Final Report and a copy of any published material arising from the project, either in full or abstract, must be provided at the end of the project.

Yours sincerely

Katherine Shaw
Executive Officer
Tasmania Social Sciences HREC

Appendix C

Information sheet



Faculty of Health, University of Tasmania

Information Sheet (H0016857)

Investigating neural mechanisms of visual attention with eye tracking technology

1. Invitation

You are invited to participate in a research study looking at how the brain implements mechanisms of visual attention. This study is being conducted by Jason Satel, School of Medicine (Psychology), UTAS.

2. What is the purpose of this study?

The aim of the proposed study is to investigate how different mechanisms in the brain interact when we are looking at a visual scene. For example, if there is a bright flash in front of you, you often can't help but look at it immediately. However, if the same object keeps flashing over and over, you will adapt and stop paying attention to it. We are interested in how these sort of effects actually work in the brain?

3. Why have I been invited to participate?

You are eligible to participate in this study if you are over the age of 18 and have no existing uncorrected visual disabilities or psychiatric/neurological disorders. Corrected vision through the use of glasses or contact lenses still makes you eligible to participate. All participation is voluntary and there are no consequences either personally or academically if you do not wish to participate.

4. What will I be asked to do?

You will be asked to conduct a series of eye movements and manual responses while completing a computerized task. Your eye movements will be tracked throughout the experiment and your brain activity and reaction times will be recorded. The experimental session should last around 90 minutes, and will take place in room N121 at the Newnham campus.

5. Are there any possible benefits from participation in this study?

Although there are no direct potential benefits participants or the wider community the study aims to gather knowledge into neural mechanisms underlying visual attention. As compensation for participation, participants will be offered the choice of course credit (1 point/hour) or a dollar value for their time (\$15/hour).

6. Are there any possible risks from participation in this study?

You may experience fatigue over the time of the experiment, if so you may inform the researcher of your discomfort and a break can be scheduled where possible. You may also experience mild skin irritation from the application of conductive gel used during electrode setup if your skin is particularly sensitive.

7. What if I change my mind during or after the study?

You are free to withdraw at any time where there is no obligation to complete participation and no explanation is needed if you choose to withdraw.

8. What will happen to the information when this study is over?

All data collected during this experiment will be confidential and will be destroyed after 5 years.

9. How will the results of the study be published?

At the end of the study, results will be published in academic journals. You can access such articles through the UTAS academic websites.

10. What if I have questions about this study?

This study has been approved by the Tasmanian Social Sciences Human Research Ethics Committee. If you have concerns or complaints about the conduct of this study, please contact the Executive Officer of the HREC (Tasmania) Network on +61 3 6226

Appendix D

Consent Form



Faculty of Health, University of Tasmania

Consent Form (H0016857)

Investigating neural mechanisms of visual attention with eye tracking technology

1. I agree to take part in the research study named above.
2. I have read and understood the Information Sheet for this study.
3. The nature and possible effects of the study have been explained to me.
4. I understand that the study involves paying attention and looking at or ignoring visual stimuli on a computer screen.
5. I understand that participation involves no foreseeable risks, other than the possibility of mild skin irritation during the application of electrodes.
6. I understand that all research data will be securely stored on the University of Tasmania premises for five years from the publication of the study results, and will then be destroyed.
7. Any questions that I have asked have been answered to my satisfaction.
8. I understand that the researcher(s) will maintain confidentiality and that any information I supply to the researcher(s) will be used only for the purposes of the research.
9. I understand that the results of the study will be published so that I cannot be identified as a participant.
10. I understand that my participation is voluntary and that I may withdraw at any time without any effect.
11. I understand that I will not be able to withdraw my data after completing the experiment as it has been collected anonymously.

Participant's name: _____

Participant's signature: _____

Date: _____

Statement by Investigator

☐ I have explained the project and the implications of participation in it to this volunteer and I believe that the consent is informed and that he/she understands the implications of participation.

Investigator's name: _____